Universidade de Aveiro Secção Autónoma de Ciências da Saúde
Ano 2014

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UMA PERSPETIVA SOBRE ASSUNTOS MÉDICOS (A CLOSER LOOK AT MEDICAL AFFAIRS)

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Tese apresentada à Universidade de Aveiro para cumprimento dos requisitos necessários à obtenção do grau de Mestre em Medicina Farmacêutica, realizada sob a orientação científica do Doutor Bruno Gago, Professor Auxiliar Convidado da Secção Autónoma de Ciências da Saúde da Universidade de Aveiro.

Dedico este trabalho aos meus pais, por terem sempre contribuído para a minha educação e fomentado a minha formação contínua, e também à minha namorada, que sempre me apoiou e incentivou a concluir este mestrado em Medicina Farmacêutica.

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o júri

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palavras-chave

Assuntos Médicos, Indústria Farmacêutica, medicamentos.

resumo

No decurso dos últimos 10 anos, a Indústria Farmacêutica (IF) tem estado sob grande escrutínio por parte das Agências Regulamentares, profissionais de saúde e doentes no geral, sobretudo por ter sido criticada no passado pelas suas táticas de marketing e vendas agressivas e comportamento não ético.

De forma a aumentar a transparência tanto das atividades desenvolvidas como da sua relação com os médicos, a Indústria alterou significativamente a forma como desenvolve e promove os medicamentos e dispositivos médicos. Muitas destas alterações levaram a uma maior responsabilização dos Assuntos Médicos (AM) na informação prestada à comunidade de prestadores de cuidados de saúde sobre o perfil de segurança e o uso apropriado dos medicamentos de uma empresa farmacêutica. Adicionalmente, verifica-se uma tendência para limitar significativamente o acesso dos delegados de informação médica aos prescritores, que tradicionalmente eram o veículo de informação da Indústria, substituindo-os por colegas imparciais especializados nos medicamentos (os colegas de Assuntos Médicos).

Grande parte desta atividade informativa envolve estabelecer e desenvolver relações de longa duração com líderes de opinião numa determinada área terapêutica de interesse. Estas parcerias científicas são cruciais para a melhoria dos resultados em saúde que as companhias farmacêuticas pretendem alcançar.

Os métodos utilizados pelos AM para comunicar ciência são diversos, abrangendo publicações em jornais com revisão por pares, congressos, sessões de educação médica contínua e grupos de discussão. Recentemente, os meios digitais passaram a ser também mais utilizados para envolver profissionais de saúde e doentes nesta partilha científica.

Os AM impactaram significativamente o relacionamento com os clientes e continuam a construir uma relação de confiança e valor, de transparência, de discussão franca sobre benefícios e riscos e promovendo um diálogo clinicamente robusto entre pares.

A atividade dos AM, que ajuda a colmatar as necessidades dos doentes e médicos e promove o uso correto dos medicamentos, contribuirá para melhorar a reputação da IF.

keywords

Medical Affairs, Pharmaceutical Industry, medicines.

abstract

Over the last 10 years, the Pharmaceutical Industry has been under great scrutiny from regulators, healthcare professionals (HCPs) and patients in general, as in the past it was criticized for the use of aggressive sales and marketing tactics and unethical behaviour.

To increase the transparency on the activities developed and its relationship with physicians, it has undergone significant changes in the way that it develops and markets medicines and medical devices. Many of these changes have led to an increase in the responsibility of Medical Affairs to inform the healthcare professionals' community on the safe and appropriate use of the company´s medicines. Additionally, there is a trend to greatly limit physician access to traditional sales representatives who traditionally were industry's vehicle of information and replace them by unbiased subject matter experts, the Medical Affairs colleagues.

Much of this communication activity involves engaging and developing long-term relationships with key scientific opinion leaders in the disease area of interest. These scientific partnerships are crucial for the improvement of health outcomes that the pharmaceutical companies aim to achieve.

The methods used by Medical Affairs to communicate the science vary from manuscripts in peer-reviewed journals, to congresses, continuous medical education meetings and discussion groups. More recently, digital channels have also been more frequently used to engage HCPs and even patients in this scientific exchange.

Medical Affairs have significantly impacted the relationship with customers, continuing to build trust and value, transparency in all engagements, providing a balanced discussion of benefits and risks, and leveraging clinically robust dialogues on a peer-to-peer level.

Medical Affairs activity, helping to address patients and physicians' needs and promoting the appropriate use of medicines, will contribute to improve the reputation of the pharmaceutical industry.

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I – INTRODUCTION

Traditionally, pharmaceutical industry model includes two main pillars: a R&D group in charge of developing new medicines/medical devices and a commercial team in charge of marketing and selling those products. However, over the past decade, the pharmaceutical industry has been under great scrutiny by regulatory authorities, with stricter legislation and frequent inspections and audits, as well as under market pressure to produce new medicines more rapidly.

Despite these many changes, all the stakeholders continued to demand that high levels of scientific rigor should be maintained across the industry and in its interactions with healthcare professionals. As a consequence of this, the urge to create Medical Affairs teams was renewed.

Medical Affairs originally appeared due to the need of having non-promotional, unbiased scientific communication to healthcare professionals, clearly independent from the commercial functions, while maintaining a bridge between research and development (R&D) and commercialization. Consequently, Medical Affairs has become an independent department/division, within the Medical Department.

In the past, pharmaceutical companies considered Medical Affairs just a support function, and one that could even slow down marketing and commercial activities. Nowadays, this point of view is completely obsolete and as, for instance, Sales teams are shrinking, Medical Affairs teams are assuming new responsibilities and generating a real competitive advantage. They are now in charge of providing scientific and clinical expertise to support approved medicines, and working closely in the development of new drugs as early as phase 2 studies and throughout post approval activities.

Furthermore, in a fast moving market environment, dynamic, innovative, engaging, and skilled Medical Affairs teams are better prepared to respond to customer demands and to develop and maintain stronger long-term relationships with key opinion leaders, scientific societies, payers and patient groups. All of this while keeping a link between R&D and commercial areas and focusing on the internal customer.

II – THE MEDICAL DEPARTMENT

The objective of all pharmaceutical companies is to discover, develop and commercialize medicines with favorable risk/benefit ratio, which benefits the patients and are profitable to the company. To ensure that this happens, it is critical to have a medical and scientific oversight since early stages of drug development and up to loss of exclusivity. The Scientific Director provides this governance within the company.

Every pharmaceutical company has a Scientific Director. Usually this person holds a degree of Medicine (doctor of medicine – MD) although a degree in pharmacy (doctor of pharmacy – PharmD) is also feasible, although less common. Nevertheless, due to the diversity and complexity of the activities developed by a pharmaceutical company, and the need to provide adequate support to several areas in a cross-functional way, a Medical Department is often put in place. Its dimension is usually adjusted to the size of the company, whether it is a multinational or a small biotechnological one. Even the way it is organized varies, and it can assume a horizontal, vertical or mixed hierarchical structure, with simple or complex lines of reporting. It greatly depends on cultural issues and different regulatory settings across countries.

The major areas of responsibility for the Medical Department are to:

- Provide a medical perspective and support to the development of new medicines (collaborating since the early phases up to phase IV clinical studies);
- Provide the medical input necessary to support marketed medicines throughout their life cycle;
- Provide specialized medical expertise, as required;
- Contribute to implementation of regional and local product strategies;
- Ensure the compliance with all applicable legal requirements, standard operating procedures and guidelines;
- Ensure that the overall drug safety reporting process fully adheres to applicable requirements;
- Perform internal audits and quality reviews;
- Identify risks from a medical point of view and implement risk management activities;

- Develop educational activities (for internal and external customers);
- Review promotional, educational and corporative materials;
- Act as the ethical conscience of the company;
- Act on behalf of the company next to Regulatory and Health Authorities, healthcare professionals and other external stakeholders;

Usually the Medical Department is staffed with the following key players:

- Medical Director;
- Clinical research specialists;
- Medical information specialists;
- Medical/scientific advisors and medical science liaisons (Medical Affairs team)
- Regulatory affairs specialists;
- Drug safety/pharmacovigilance specialists

The Medical Department is headed by the Medical Director (usually a physician), who leads a team of other physicians, pharmacists or life scientists and administrative staff. They all play an important role supporting all phases of a medicine life cycle, from early stages of development until the loss of exclusivity (LOE), always partnering with commercial colleagues.

III – IMPORTANCE AND ROLE OF MEDICAL AFFAIRS

Medical Affairs is a global function. Nevertheless, Global Medical Affairs has a very limited role in country or region-specific activities because issues and regulations differ across markets. Global Medical Affairs defines a broad overall strategy and ensures that the activities across markets are aligned and that redundant efforts are avoided. It may also take the lead on activities that can truly span all markets, such as:

- publication planning;
- fostering long-term relationships with internationally recognized key opinion leaders;
- draw general guidelines for selecting which studies to fund (company owned or from investigator-initiative research);
- defining real-world data and outcome research needs;
- global advisory board.

Because Medical Affairs works closely with both scientific and commercial leaders within a pharmaceutical company, the function could be positioned under either Global Commercial or Global Development.

However, as regulatory scrutiny has increasingly highlighted the need for a clear separation of commercial and educational/scientific activities, Global Medical Affairs has been generally aligned with Development (or sometimes in a direct reporting relationship to the CEO of a pharmaceutical company. It is also becoming more common for Medical Affairs to derive its budget from Drug Development rather than from Marketing.

As mentioned previously, Medical Affairs is a division within the Medical Department. It typically interacts with many different players, both internal and external. Regarding internal customers, it interacts with marketing, regulatory affairs, clinical research, medical information, pharmacovigilance, quality & compliance, access, sales, and legal. Considering external customers, the Medical Affairs team establishes straight, peer-to-peer interactions between collaborators from the pharmaceutical company and healthcare professionals, mainly physicians, scientific societies and payers.

In larger pharmaceutical companies, reporting to the Medical Director, there can be also a Medical Affairs Lead/Director. This person usually has a degree in medicine (MD) although a degree in pharmacy (PharmD) is not uncommon. Apart from the director, Medical Affairs typically are staffed with medical managers/advisors and scientific advisors (both office based) and medical science liaisons – MSLs (who are field based), both of which are customer facing roles, but at different extents.

Regarding the scientific background of people working in Medical Affairs (usually MDs, PharmDs, or holding any advanced master degree in life sciences), these are highly differentiated employees with in-depth knowledge of the therapy area, the relevant medicines in the company portfolio and its pipeline, capable of dealing with extremely complex scientific/technical information, which enables them to understand and effectively communicate the science behind a medicine or medical device.

Considering that a drug emerging from clinical development and on route to enter commercialization may be, to a considerable extent, "unknown" to potential prescribers and other healthcare professionals, Medical Affairs spearheads efforts to explain the "real world" utility of this new drug through the dissemination of unbiased clinical and scientific information about it. Although Medical Affairs has traditionally focused on communications with healthcare professionals (people who make use of the drug), nowadays this information is increasingly important to payers as well (Governments, Health Ministries, Hospital Boards, insurance companies, etc).

Internally, Medical Affairs often serves as a "bridge" between the research/clinical development and commercial divisions of a pharmaceutical company (or of a biotechnology company with in-house commercial capabilities), synthesizing information and translating findings about a drug into language accessible to company professionals whose primary expertise is not necessarily scientific.

Overall, the responsibilities of a Medical Affairs team may include:

- Perform in-country clinical studies feasibilities. Countries are often challenged about their capability to run clinical studies and Medical Affairs' in-depth

knowledge of the national clinical setting and reality allow them to rapidly identify potentially interested centers and investigators.

- Conducting non-registrational (typically Phase IV) clinical studies. After a drug wins EMA approval, Medical Affairs often assumes much of the responsibility for any additional clinical studies. Because these studies do not support the application for approval, they are known as non-registrational studies.
- Medical Affairs also supports investigator-initiated studies. Medical Affairs reviews the clinical study proposals submitted by independent investigators and decides based on their scientific merits, which of the studies should receive financial support.
- In addition to non-registrational studies, Medical Affairs is sometimes responsible for executing health economics and outcomes studies, in partnership with the Access department. These studies, which evaluate the impact of a drug use on such variables as overall medical costs and patient quality of life, can be used to "make the case" with health plans and prescribers that a drug's value (financial and humanistic) exceeds its cost.
- Medical Affairs may also be responsible for supporting the Brand team in formulating product messages. Insights from Medical Affairs help Brand teams to develop clear and scientifically accurate promotional materials. They also develop and/or review scientific/medical content that is converted into training materials, for use with the Sales, Marketing, and enabling functions teams.
- In the course of its outreach to the medical community, the Medical Affairs team learns a great deal about the market environment for company products and can share this knowledge with internal leaders, such as, product messages that are responsive to the concerns of prescribers and other key stakeholders.
- Medical Affairs also plays an important role in disseminating written information to the scientific community. One major contribution of Medical Affairs in this area is defining the publication plan for each product. It also coordinates clinical and scientific communications disseminated by the company at medical congresses.
- Members of the Medical Affairs "field force", commonly called Medical Science Liaisons, are responsible for outreach to key opinion leaders (KOLs) —

often the foremost researchers in their fields of expertise. KOL insights and involvement are often critical to development of a successful product.

- Medical Affairs may sponsor (or lead the development of the sponsorship strategy for) external education programs for healthcare professionals, particularly in areas of focus within the company product portfolio.
- Another core activity of the Medical Affairs function is to respond to unsolicited product inquiries from healthcare professionals and (to a lesser extent) patients. The volume of calls is highest around the time of the market launch of a new drug or following a major change in a drug's approved prescribing information.
- Medical Affairs is also important to help identify new business opportunities, unmet scientific/medical/patient needs and to contribute to challenge the *status quo* and suggest improvement actions, both for internal or external customers.

In conclusion, the role of Medical Affairs within a pharmaceutical company serves to spearhead the dissemination (and in some cases the generation) of unbiased clinical and scientific information about a medicine (to be launched or already on the market) to the healthcare community and to offer medical and scientific expertise to support the Brand teams. In the course of executing these duties, members of the Medical Affairs team gather a great deal of market intelligence. Those findings are shared internally with senior management (in country and above country).

IV – CLOSER LOOK AT MEDICAL AFFAIRS

The nine major responsibilities of Medical Affairs in a pharmaceutical company include:

a) Product research and development

The nature of Medical Affairs involvement in product research and development varies by stage of the product life cycle. The involvement of Medical Affairs in development of a drug that has not yet been approved for marketing by EMA is typically modest compared to its role once EMA approval has been granted. Its earlier contributions can, however, have a major impact.

For instance, during the preclinical phase of drug development, Medical Affairs provides valuable perspective based on its understanding of alternative products and unmet needs. This insight can help produce a drug that addresses limitations in the current standard of care.

Regarding resource allocation, phases III and IV are the major responsible for resource consumption, which typically corresponds to the peri-launch period of a medicine.

The Medical Affairs team can help other stakeholders explore pivotal questions including:

- What is the target population for the product? Adult, pediatric, geriatric?
- What is the relative importance of various product characteristics? Is there any trade-off to be made (e.g. dosing regimens)?
- Is it important that a drug has a particular mode/route of administration?
- Is it important that a drug reduces the incidence of a particular adverse event, such as nausea?

Clinical development conducts all the clinical studies that directly support the product's label for marketing approval. These are called registrational studies, because they gather the data upon which EMA makes its approval decision. They include Phases I, II, and III clinical studies.

The assistance Medical Affairs provides during these studies is primarily related to identification and recruitment of study investigators. Its "field force" of MSLs can leverage contacts among key opinion leaders at the forefront of clinical research in order to aid investigator and site recruitment efforts. The Medical Affairs team may also continue to provide input regarding desirable product attributes from a prescriber and patient perspective.

After a drug has won regulatory approval, Medical Affairs often assumes responsibility for subsequent clinical studies. Because these post-approval studies, also referred to as post-marketing or Phase IV studies, are not the basis for regulatory approval, they are considered non-registrational. These studies are typically large and community-based.

They may also be observational in nature, that is, they track the clinical status of patients who have been prescribed a drug, without intervening in treatment. Although the primary focus for most Medical Affairs departments is Phase IV studies, in some pharmaceutical companies they may also assume primary responsibility for what are

known as Phase III B studies (those conducted after a submission to regulators for marketing approval and aiming an additional indication/label).

There are a number of reasons to conduct non-registrational studies to supplement the information that formed the basis for EMA approval. These reasons include:

1) Gathering additional safety information.
    - As Phase III studies often include selected patients due to its strict inclusion criteria, once a new drug is on the market Phase IV studies are important to assess safety in a larger population, in specific subpopulations, or simply across a longer time span. Such information may be considered particularly important when a product has been granted accelerated approval to expedite patient access to an urgently needed therapy. This form of post-launch safety surveillance can detect rare adverse events and help clarify the frequency with which known adverse events occur.

2) Enhancing product differentiation.
    - Non-registrational studies also gather additional information related to product differentiation. The clinical data submitted for EMA approval, does not usually demonstrate the product's full therapeutic value and its areas of distinction from competitors. A Phase IV study may supplement available data by, for instance, assessing results in a specific user segment to evaluate whether outcomes within that subpopulation are superior to outcomes in the broader population for which the drug is indicated.

3) Evaluating product use in a variety of "real-world" settings.
    - The subjects in registrational studies whose behavior is carefully tracked under the ideal conditions of a clinical study may behave differently than people taking the commercialized drug would. Phase III B and Phase IV studies can yield practical data about patient response when the drug is prescribed in a more typical setting, such as a routine physician office visit. One question might be, "is compliance with the recommended

treatment high or low?" These studies are also an opportunity to gather additional outcomes data for analysis by the Health Economics and Outcomes group. Such studies also introduce the product to new prescribers who might not otherwise become aware of its benefits to their patients.

4) Increasing local market presence and experience.
    - In addition to gathering information related to "real-world" use, non-registrational studies may also be leveraged to increase local market presence. A pharmaceutical company may choose to replicate a global study in a local market. Such studies can both confirm a product's efficacy and safety and provide local investigators who were not part of the global study an opportunity to participate in a product-related study. These studies may also permit comparison of the drug's performance to the standard of care in that particular market.

In most pharmaceutical companies, Medical Affairs focuses mainly on Phase IV post-marketing studies of approved indications, while Clinical Development executes other clinical studies. In some instances, Medical Affairs may also be involved in the ongoing evaluation of new opportunities for drug use, which are "off-label" studies. The term "off-label" can encompass any change to the regulator-approved language regarding use of a drug, up to an entirely new indication.

If results from an off-label study of a new indication are sufficiently promising, a pharmaceutical company may make the very large investment required to execute additional Phase II and Phase III studies in order to obtain regulatory approval. Clinical Development is likely to assume responsibility for this new cycle of Phase II/III studies.

Promotional use of the information gathered during off-label studies is prohibited. Medical Affairs colleagues can, however, provide some information about off-label studies in a reactive way, upon unsolicited request by a healthcare professional. Additionally, pharmaceutical companies are under a duty to publish their findings in peer-reviewed journals, so that both positive and negative data are available and effectively disclosed to the scientific community.

Phase IV studies initiated by a pharmaceutical company may be driven by interest in gathering additional product information or by a mandate by regulators to gather additional safety data. Investigator-initiated studies are typically smaller in scope. Their impetus is the interest of a leading physician or group of physicians in a new treatment approach, or a variation in some standard part of a drug therapy, such as a route of administration, dose, or dosing schedule. To help them make more informed prescribing decisions, some physicians may want to evaluate how different therapies perform “head to head.”

b) Investigator-initiated studies

Phase IV studies initiated by a pharmaceutical company may be driven by interest in gathering additional product information or by a mandate by regulators to gather additional safety or real-world data. Investigator-initiated studies are typically smaller in scope. Their motivation is the interest of a leading physician or group of physicians in a new treatment approach, or a variation in some standard part of a drug therapy, such as a route of administration, dose, or dosing schedule. To help them make more informed prescribing decisions, some physicians may want to evaluate two different therapies “head to head.”

In investigator-initiated studies, the physicians proposing the study are responsible for the study conduct, the integrity of study findings, and adverse events reporting. Investigators will sometimes request support for their clinical studies from the pharmaceutical company that manufactures the drug that will be studied. If the company agrees with the scientific merits of the proposal, it may choose to provide some product (medicine or pure substance) and/or financial assistance. This support may include free donations of the drug (particularly important contribution when the drug is highly expensive). The company cannot, however, be involved in any way in the actual conduct of an investigator-initiated study. The conclusions drawn from the study must be the independent judgment of the investigators.

c) Health economics and outcomes studies

Health economics and outcomes studies usually are on the dependency of Market Access, especially in bigger pharmaceutical companies, and are critical to supporting the product value proposition. However, this analyses can also be performed by Medical Affairs for such purposes as: demonstrating the financial and quality-of-life impacts of a disease, the limitations of other therapies (including the existing standard of care), and the differentiating characteristics of a medicine/device in terms of cost and patient outcomes. Health economics and outcomes data are often critical to effective positioning with payers and health plans. They can also influence the prescription preferences of physicians.

Health economics studies focus on the cost-benefit equation in purely financial terms. For example, they may evaluate the total cost per treatment episode of a company product, sometimes in comparison to the cost per treatment episode for another drug or therapeutic regimen, or if the use of the drug reduces the need for more expensive interventions such as hospitalizations.

A drug with compelling proof of health economics or outcomes benefits is likely to be treated more favorably than a drug without it. This information can be used to influence payers and health authorities when they are making decisions about which drugs in a treatment category should have the best positioning on their formularies (the list of drugs they prefer to use). Medical Affairs teams can also use such evidence with prescribers, discussing the specific cost-benefit of a drug compared to other(s) in the treatment of a disease.

Typically, these studies are performed as a retrospective analysis. The data utilized often comes from preexisting external resources, such as clinical studies, observational studies and prescription databases. Data sources may also include findings from the company's own clinical studies. Preexisting data sets may not, however, answer all the treatment and outcomes questions that a pharmaceutical company or a payer considering its products would like to be addressed. In some cases, in order to gather specific information of interest, it may be necessary to conduct a prospective study and detailed analysis of the outcomes/results.

One way of conducting a prospective study is setting up a patient registry that screens future participants based on customized inclusion and exclusion criteria. The critical benefit of such analyses is the ability to specify the exact characteristics of study subjects and the precise data to be tracked. Unlike clinical studies, patient registries are solely observational in nature. They track the therapy provided to patients and their ongoing health status, but do not intervene to change healthcare practices.

In some cases, analyses of patient registry data or of preexisting clinical study data may show the unmet needs of the treatment or minimize regulatory safety concerns. If unexpected health issues become apparent, however, regulators may change the labeling for the drug or drug class. In the absence of robust and reliable registrational data, clinicians who develop treatment guidelines may rely upon published health economics and outcomes studies as a basis to define the standard of care.

d) Supporting the Brand team

Medical Affairs is a valuable channel of clinical and scientific information to a pharmaceutical company's commercial leadership. Although it is important to be clear that it is the Brand team, and not the Medical Affairs team, which defines promotional product messages, Medical Affairs can assist the Brand team by offering medical and scientific insights into the product's value proposition.
A huge quantity of data is typically generated in the course of a drug's development. The Medical Affairs team synthesizes that data and provides commercial leaders with key findings in a way that they can easily understand without great depth of scientific or clinical expertise.

The contributions of Medical Affairs often go beyond supplying the key clinical findings. Medical Affairs can offer feedback on the product's strengths and differentiating attributes. Its experts may also help guide discussions regarding the need for additional clinical studies and health economics and outcomes analyses, by identifying the data required to provide a compelling demonstration of key differentiating attributes; the gaps in currently available data; and the means of filling

those gaps. Medical Affairs may also offer special insight into the strengths and weaknesses of competing medicines.

The Medical Affairs team may also be part of a promotional review committee, helping the Regulatory, Compliance and sometimes Access and Legal teams to verify the content accuracy of the messages developed by the brand team and their consistency with EMA-approved language in the label.

In addition, the Medical Affairs team provides materials and information to support the training of the company's "field force." The team creates scientific and medical content (and/or reviews the content created by outside vendors) in order to help the Brand/Sales team(s) develop course materials for the Sales Representatives. The content is focused exclusively on scientific/medical aspects of the products and therapeutic area, not commercial messaging.

At last, they can help put together Advisory Boards, meetings where a usually heterogeneous group of experts can freely discuss and provide credible advice on a predetermined subject (or simply to provide a more comprehensive overview of the environment), based on their clinical practice or scientific knowledge, in a closed setting. This can be very important for the Brand team, which is able to make adjustments to its strategy.

e) Publication planning

The Medical Affairs team is responsible for disseminating accurate, complete, and unbiased non-promotional information about company products and/or about the drug class and disease states that are of interest to the company (based on its current or future pipeline). This information may relate to research, preclinical, clinical, health economics, or outcomes data.

The team designs and executes the publication plan for each product. The publication plan is a carefully synchronized effort to disseminate accurate disease state and product-

related information in order to promote product understanding within the healthcare community and, as appropriate, product adoption.

Although publication planning may be seen largely a matter of determining when and where to publish information about a product (When will the relevant data be available? When should publications and press releases be scheduled? What journal should be targeted? What assistance can we provide to the authors?), in fact it is a more strategic responsibility, with greater emphasis on defining the research data that must be generated to make the publication effort effective in conveying a product's benefits.

With respect to the publication planning strategy, Medical Affairs may ask:

- What is needed to demonstrate the value proposition?
- What are the data gaps?
- How these can be overcome/answered?
- What is our back-up strategy?
- What are competitors' data and strategies?

With respect to tactical execution, Medical Affairs may assess:

- When will data be available?
- Which journals should be approached?
- Is it better to publish in a subscription journal or go for open access?
- When can final publication be expected?

The Medical Affairs team also plays a role in medical writing related to company compounds and products, assisting with the translation of scientific and medical findings into various forms of written communication. Its involvement may begin as early as the research phase for a drug and continues across the product life-cycle. The team may draft or assist in the development of materials including the following:

- Journal articles (manuscripts)
- Abstracts (summaries of published articles)

- Posters (oversized summaries of preliminary study results, which key opinion leaders present at medical conferences and in other settings, in what are known as “poster sessions”)
- Review articles (that synthesize all published research materials)

While the Medical Affairs team may assist investigators on company-sponsored clinical studies with drafting and revising publications, a highly rigorous standard is applied to ensure that the named authors merit that status based on their contributions to a work.

f) Relationships with Key Opinion Leaders (KOLs)

Key opinion leaders (KOLs), also referred to as thought leaders, are highly respected experts in their clinical fields. Each therapeutic area typically has its own KOLs. Often, they are the foremost researchers in a particular therapeutic area. They may also be the editors or contributors to key journals in their area of specialization. Some KOLs are also involved in professional scientific societies.

Regardless of their precise role, KOLs exert strong influence over other healthcare professionals. Their assessment of various treatment options carries great weight with community physicians deciding among therapies, and influences future prescribing patterns of physicians training in their institutions. It is therefore important to enlist the expertise of these KOLs in the development of new drugs.

Pharmaceutical companies build and maintain KOL relationships for a variety of reasons, all related to their clinical expertise and the respect their peers have for their perspectives on a particular therapeutic area. What is the advantage for the company?

- First, KOLs can offer insights into treatment issues and unmet needs in the therapeutic area, which may allow pharmaceutical companies to focus their clinical development efforts.
- Second, KOLs may agree to contribute as investigators on clinical studies for company products, thereby increasing the impact of such studies on the

perceptions of other healthcare professionals. They may then agree to present findings from the clinical studies in which they were involved.

- Third, KOLs provide disease-state education to their fellow physicians, building awareness of the need for diagnosis and the options available for treatment.
- Finally, KOLs may educate peers/other physicians about the therapeutic options they consider best. Based on their independent medical analysis, KOLs may choose to recommend the class of drugs to which the company's product belongs.

Medical Science Liaisons (MSLs) within the Medical Affairs team are responsible for cultivating long-term relationships with key opinion leaders. Like Sales Representatives and Account Managers, MSLs work primarily out in the field. They routinely call upon medical centers, teaching/public/private hospitals and individual KOLs. In many cases, the KOLs are affiliated with one renowned medical institution.

By fostering KOL relationships, MSLs can provide support for both non-registrational and registrational clinical studies, as they identify, evaluate, and help recruit potential study sites and also study investigators (physicians who may lead clinical studies at particular sites).

Like other members of the Medical Affairs team, MSLs usually have extensive clinical or research experience in the therapeutic area with which they are associated. They have a medical degree, a doctorate in pharmacy, a doctorate in a field such as biology or epidemiology or some other degree reflecting deep expertise related to complex medical and scientific issues.

Because MSLs communicate science in an unbiased manner, they are often recognized as "peers" by physicians, and their input and advice are highly valued. Healthcare professionals are often overwhelmed by people who want to speak with them about their products. For Sales Representatives, it is quite hard to win even a brief period of "face time" with a physician, particularly a KOL, while MSLs are more likely to gain access and their discussions with KOLs and physicians are often lengthy.

The success of a MSL in securing access is often tied directly to his or her demonstrated mastery of the latest research data related to a therapeutic area, disease state, and drug. Clinicians often welcome the opportunity to meet with people whom they perceive as unbiased experts who are equipped to respond to both on-label and off-label queries.

In addition to conducting these routine "field" visits themselves, MSLs are also available as an expert resource for the Sales teams. As requested, they will present scientific and/or health economics data to key prescribers and payers. Typically, prescriber presentations take place at hospitals or in multi-client settings, such as conferences/congresses. In most cases, MSLs will not appear together with Sales Representatives, in order to eliminate any link to the commercial area, as well as to retain the independency of their role and the information they share.

The MSLs are not only available for presentations but "on call" for expert consultation, when Sales teams or Account Managers need an interpretation of scientific or clinical information, as they are particularly well equipped to respond to complex queries.

In some organizations, the MSLs can also interact with key customers at important hospitals/health authorities, such as clinical (medical) directors and formulary committees, or working in professional scientific societies, who are critical influencers regarding product inclusion in hospital/national formularies and guidelines.

g) Medical Education and Training

The Medical Affairs team may support both internal training and the sponsorship of external education programs.

Internal training by Medical Affairs is not limited to education of team members within the function, teaching the scientific knowledge and the communications skills necessary to their roles but also teaching colleagues from Marketing, Sales team and enabling functions about a specific disease area/pathology or medicine, in order to increase their knowledge about it.

Sponsorship of external education programs is a critical responsibility of the Medical Affairs team. Medical Affairs sponsors continuing medical education (CME) programs, medical conferences, and symposia at which healthcare professionals in selected therapeutic areas gather. Medical education programs are selected based on relevance to therapeutic areas and disease states of importance to the company, as well as the interest key opinion leaders and other healthcare professionals have for the programs.

Medical Affairs also sponsors speakers programs, at which healthcare professionals from outside the pharmaceutical company share information regarding the disease state, therapies, and ongoing research findings. All such programs should be a means of presenting an unbiased perspective on the disease states and available therapeutic options.

A typical speakers program may consist of one or more key opinion leader(s) (doctor or pharmacist) meeting exclusively with fellow healthcare professionals. Possible topics of discussion include the merits of various therapies, current research findings from ongoing clinical studies or strategies on how to improve patient adherence to the medication. Some speakers programs, however, are modest community-based initiatives that provide information about treatment options to patients as well as healthcare professionals.

To establish a greater separation of medical education from promotional efforts, there is a trend now that require Medical Affairs, and not Marketing, to control the budget and the ownership for these programs.

Finally, although Medical Affairs can specify the general topic to be cover at a sponsored educational event, the team does not exert any control over the content of those presentations, and preserves the speakers' freedom of speech.

h) Market intelligence

Medical Affairs has many opportunities to understand the clinical and market environment trends for company medicines and communicate that knowledge to

internal stakeholders so that all maintain a current understanding of the perspectives of key stakeholders. The Medical Affairs team maintains regular market awareness through:

- close contact with healthcare professionals, that reveal their product questions, concerns, and preferences;
- conversations in the "field" with key opinion leaders, who keep them updated of leading-edge investigations and unmet needs;
- company-sponsored medical education programs;
- feedback during presentations before medical audiences.

Although this information is not gathered for commercial purposes, it is a valuable resource for commercial functions striving to understand market needs and concerns. This market intelligence is highly valuable to better understand the brand and the therapeutic area.

i) Medical Information

Responding to product-related information requests may also be a responsibility of the Medical Affairs function.

Usually, this responsibility can be delegated on a specific team within Medical Affairs: the Medical Information group. This group responds to calls from other healthcare professionals, including physicians, nurses and pharmacists. Less frequently, they also receive calls from patients. The calls are usually related to questions about appropriate use, risks, benefits, and other characteristics of company products. Many pharmaceutical and biotechnology companies also train their Sales Representatives to forward all off-label clinical questions arising during client calls to the Medical Affairs team or to the Medical Information group.

For common queries, the Medical Information group may have "Frequently Asked Questions" scripts (internally pre-approved) to help them provide clear, consistent, and

accurate responses. Some companies may back their answers with a supporting letter and/or relevant literature.

In larger organizations with an array of brands and/or brand indications, the Medical Information group can act as the “first line” of healthcare professionals that perform triage and answers more common questions, forwarding more complex questions to the Medical Affairs team, namely the Medical/Scientific Advisors, for a customized response.

Calls from healthcare professionals to report adverse events in patients taking a drug are fielded by a separate function known as Pharmacovigilance or Drug Safety, which is responsible for reporting these events to regulators. During clinical studies, investigators report all such adverse events directly to the Drug Safety function. After a drug is on the market, however, such reports may sometimes be sent to Medical Information, which then triages the calls to Drug Safety. Ideally, prior to forwarding the calls, the Medical Information captures detailed information about the reported adverse events to assist Drug Safety in categorizing them and assessing their seriousness.

To be able to anticipate and respond effectively to queries, Medical Information needs to review and analyze available scientific and medical literature. To remain up to date, they monitor the literature on an ongoing basis.

V – MEDICAL AFFAIRS CORE COMPETENCES

A Medical Affairs colleague must fulfill some minimum requirements in order to maximize his/her impact on customers, both internal and external. These requirements can fall in one of two major skills: scientific and personal.

Scientific skills:

- Know-how
    - Advanced knowledge of concepts and theories in the therapeutic area(s), including competitive landscape and current medical and scientific knowledge (e.g., disease states, product label, statistics interpretation)
    - Advanced knowledge of research, including but not limited to observational and clinical study design, hypothesis testing, basic statistical methods, clinical study analyses and basic understanding of other types of research (such as outcomes research and pharmacoeconomics)
    - Significant knowledge of the healthcare environment at local, regional and national level.
- Customer focus
    - Identifies, develops, and maintains strong partnerships with regional and national medical experts, scientific societies and other decision makers
    - Builds and leverages a large network of contacts (key opinion leaders)
    - Acts and anticipates, by means of the customer, insights and needs
    - Knows how to optimally add value to a therapy area, product or service
    - Manages customer expectations by bearing in mind the business
- Entrepreneurship
    - Innovative and proactive
    - Anticipates opportunities and solves problems
- Results oriented
    - Action focused to achieve or exceed objectives
    - Business acumen
    - Uses opportunities to increase effectiveness and efficacy of services and processes
- Networking
    - Has the ability to build and maintain a large network of contacts, internally and externally with a focus on information exchange

    - Able to influence decision makers in profiling the services and products of a pharmaceutical company in the market
- Cooperation/Working together
    - Works with colleagues or customers to achieve mutual goal

Personal skills:

- Engagement
    - Proactively engages with the organization demonstrating the value of the Medical Affairs role in achieving our business objectives
    - Exerts this competency positively in all circumstances, without compromising on his own personal values
- Emotional intelligence
    - By having self and knowledge of others builds meaningful long term relations. The person has intrinsic interest in other people and acts in a way to gain trust that enables open communication
- Integrity
    - Is an example of living the company's values and procedures.
    - Takes and defends decisions being made and executes against them, even if they are not popular and controversial
- Change agent
    - Acts positively and is open to change and uncertainties, without getting reactive or being paralyzed
- Convincing others
    - Has strong written and oral communications skills and is able to present fair and balanced data effectively to both internal stakeholders and external customers, including medical experts and key decision-makers in small (1:1) or large meetings
    - Is able to motivate others

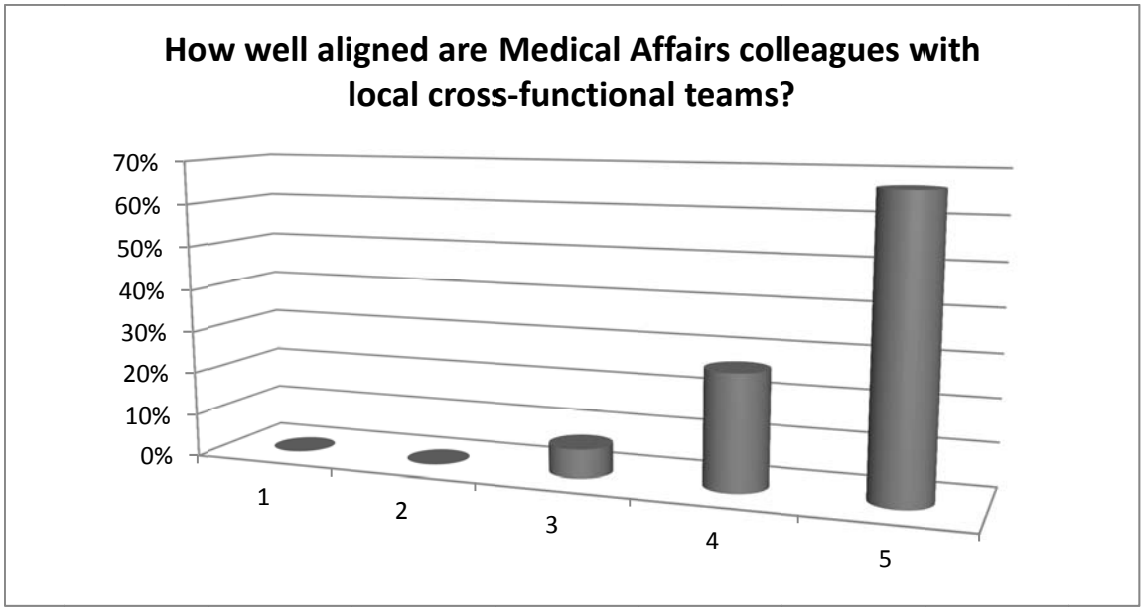
These set of skills allow Medical Affairs teams to build and develop enduring peer-to-peer relationships with healthcare professionals and institutions in order to create constructive and cross-functional partnerships with internal and external stakeholders. Acquired partnerships will generate customer insights and leverage business opportunities, providing medical/scientific support to the brand that is aligned and integrated in the overall brand strategy and clinical plans.

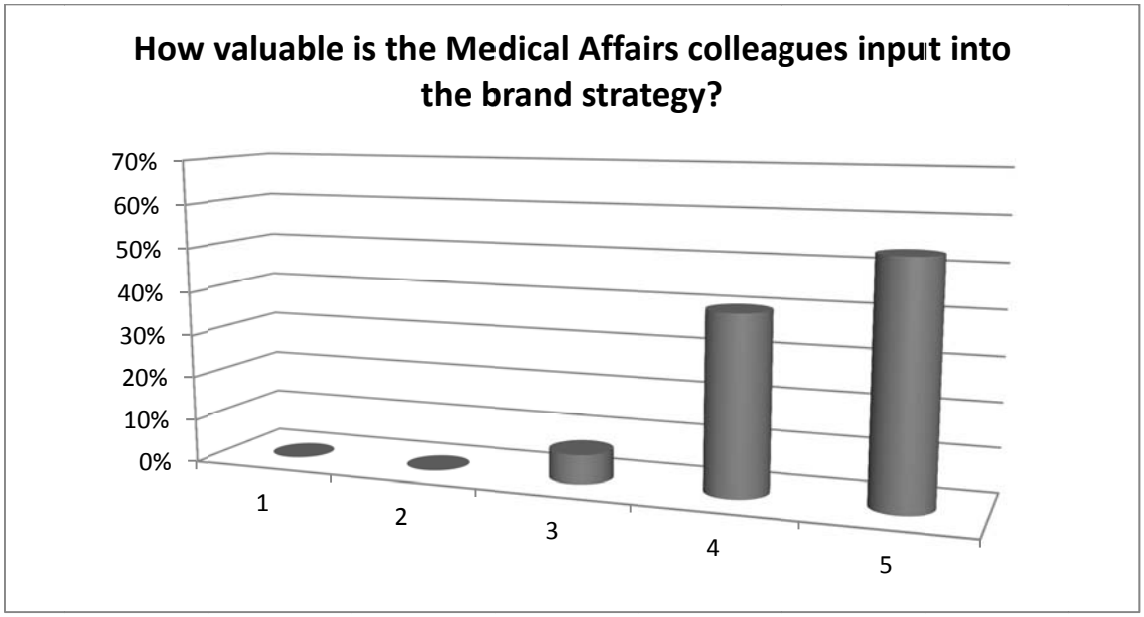
VI – HOW MEDICAL AFFAIRS ARE PERCEIVED

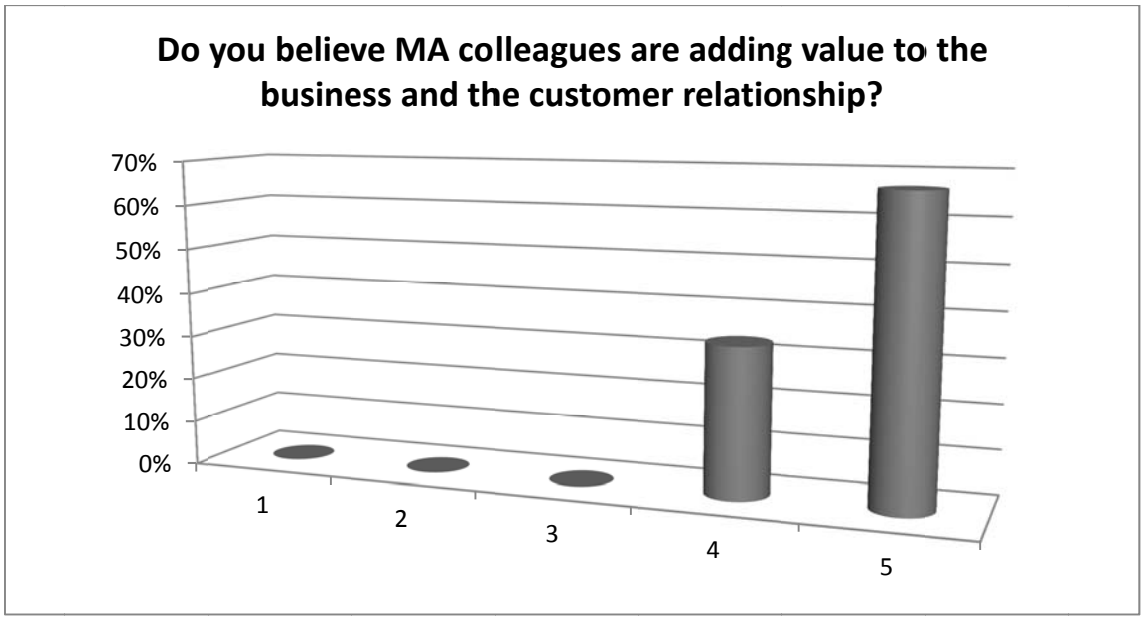
The activities developed by Medical Affairs colleagues are diverse and have been detailed above. But what is its impact? How are Medical Affairs perceived by internal and external customers? I have performed a small enquiry to address this topic (both to internal and external customers) and the results are presented below.

What do internal customers say about Medical Affairs (MA)?

- 15 colleagues (marketing, sales, regulatory affairs, access) were asked 3 questions about Medical Affairs colleagues, scoring their answers from 1 to 5.[1]



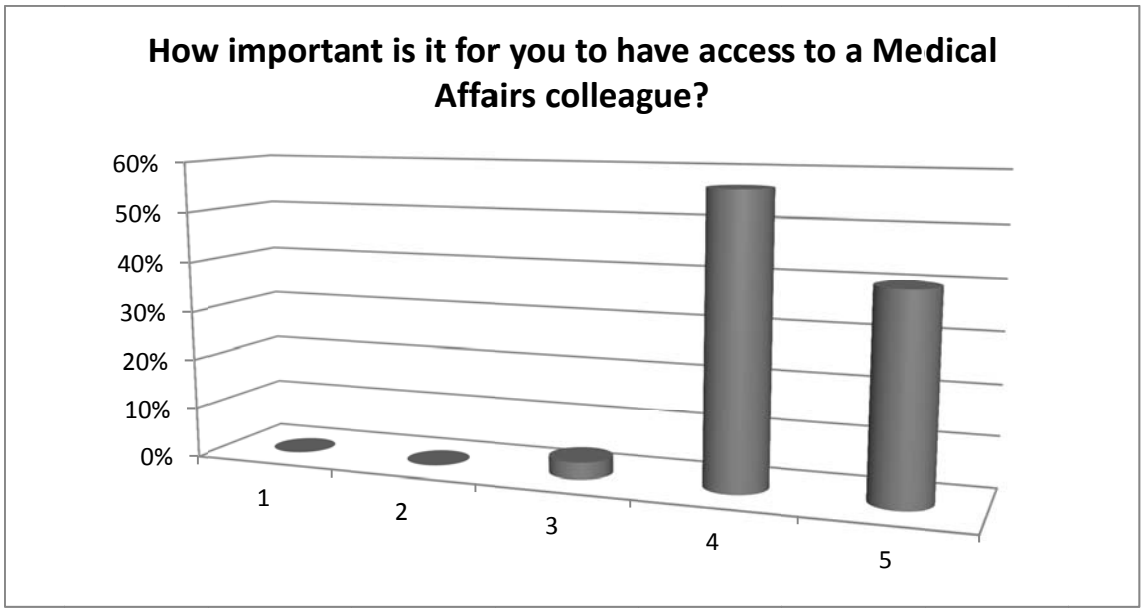


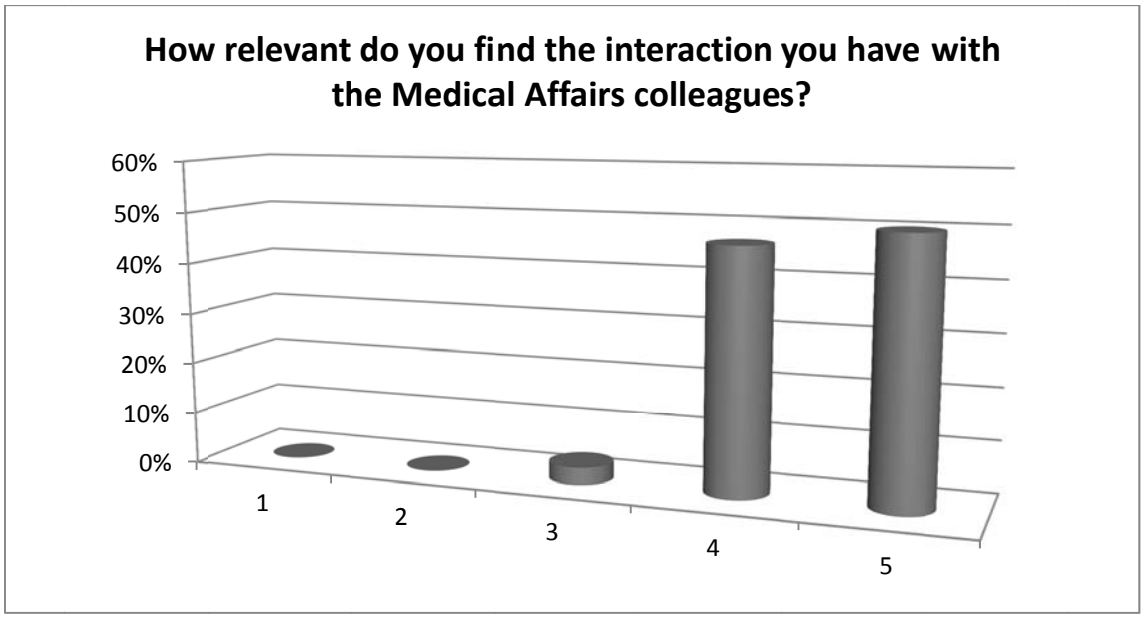


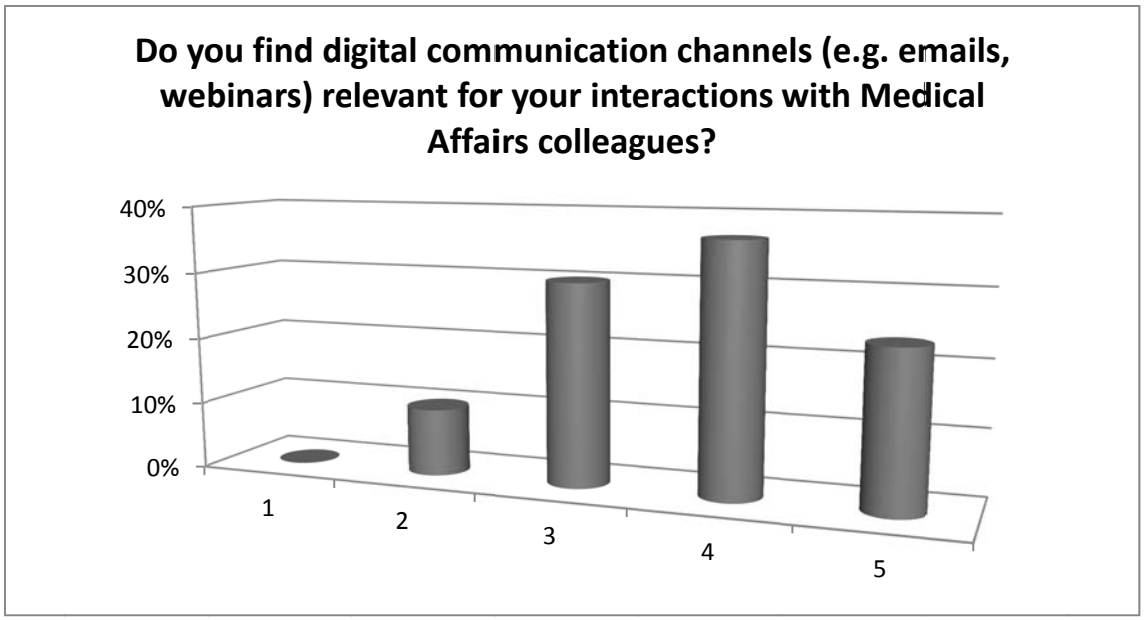
From this data, we can confirm that Medical Affairs colleagues play an important role to the company, supporting and collaborating with cross-functional teams and providing significant inputs to the brand strategy.

And what do external customers say about Medical Affairs (MA)?

- 30 key opinion leaders (cardiologists, neurologists, haematologists, internists and vascular surgeons) were asked 3 questions about Medical Affairs colleagues, scoring their answers in a scale from 1 to 5.[2]







This small (n=30) survey to KOLs also demonstrated that access to Medical Affairs colleagues is recognized as quite important and the interactions they have with KOLs are considered very relevant. KOLs also have a positive opinion about the use of digital communication channels in their interactions with Medical Affairs colleagues, although the responses were more heterogeneous, perhaps due to less developed digital communication skills or simply due to the fact they rather have face to face interactions.

VII – LEVERAGING THE IMPORTANCE OF MEDICAL AFFAIRS

Considering that the importance of Medical Affairs teams is growing, as more and more physicians recognize they are the most knowledgeable individuals to talk about a medicine within a pharmaceutical company, and they are independent, reliable and a trustworthy source of information, how can they reinforce its unbiased communication to make a significant difference in patients' lives and strengthen the peer-to-peer relation with customers? The purpose is to create, demonstrate, and communicate the clinical value of medicines in a truthful, complete, balanced and unbiased fashion:

- Enhancing knowledge of medicines and the associated therapeutic areas in which a company focus its research efforts.
- Providing thorough understanding of its medicines: interpret emerging scientific trends, clinical data and the competitive landscape and align internal stakeholders on a balanced benefit/risk proposition.
- Communicating to the medical and scientific communities in an accurate, fair and balanced manner about the benefits and the risks of the medicines, enabling prescribers and other healthcare decision-makers to take informed decisions with patients and use medicines safely and effectively.

How will the Medical Affairs team demonstrate the value of the company's medicines given the challenges posed by the market? It significantly depends on their ability to work in cross-functional teams:

- Work cross-functionally with colleagues from Marketing, Sales, Regulatory and Access to guide the acquisition and integration of clinical data so that existing clinical evidence is communicated accurately, reflecting the value of the medicines;
- Participate in regulatory strategy and engagement of regulatory agencies to ensure the clinical relevance of our medicines is well understood by regulators; communicate according to label;
- Work in label development and the rationale for label changes throughout the medicine's lifecycle;

- Work cross-functionally to establish publication planning in order to ensure timely and accurate dissemination of the company's clinical studies data to the scientific community;
- Partner actively with Market Access/Health Economics and Outcomes Research and other internal partners in designing payer strategies and engagement of payers to ensure the clinical value of our medicines is communicated properly throughout the lifecycle within the context of the existing and emerging treatment paradigm;
- Provide customer insights to help inform the differentiation of the company's medicines.

How can the Medical Affairs team collaborate to impact positively the business of a pharmaceutical company? Medical Affairs teams are the interface between clinical development and clinical practice. From before proof-of-concept to the end of the lifecycle, they engage with and guide business development, research, and clinical and commercial development. They also:

- Help to inform the right capital allocation decisions in the advancement of the lifecycle of the brands and the company's pipeline;
- Ensure launch readiness, organizing and training medical affairs colleagues and providing them with the tools to excel within the pre-, peri- and post-launch period;
- Help the business grow by informing and aligning with cross-functional colleagues on what is needed to enhance the value through the generation of additional clinical study and real world data beyond registration throughout the medicine lifecycle;
- Identify areas of unlocked value by gaining customer insights and thinking innovatively about current clinical data, treatment paradigms and healthcare environments.

VIII – CONCLUSION

Medical Affairs is a division within a Medical Department of a pharmaceutical company, established to make possible the delivery of straight, truthful, complete and balanced information and the development of peer-to-peer interactions between collaborators from the company and healthcare professionals, mainly physicians.

Its importance has arisen over the past years in response to external regulatory pressures to separate medical and commercial activities, improving the image/reputation of pharmaceutical industry. The Medical Affairs activities are all about healthcare professional education and working in partnership with them to achieve effective results, helping to address patients' needs and the appropriate use of medicines.

Medical Affairs colleagues are crucial for the pharmaceutical industry business as they:

- Are experts in what regards providing medical/scientific support to marketing/access/sales;
- Are able to deliver medical training to Sales Force or other internal colleagues about a specific disease/therapeutic area or about the medicines in the companies' portfolio in order to increase their therapeutic skills and product knowledge;
- Are competent collecting customer insights and feed it back into the pharmaceutical company to generate and leverage business opportunities;
- Can support business decisions/brand activities by setting up and coordinating advisory boards;
- Develop long-term relationships with external customers, namely key opinion leaders, scientific societies, health administrations, patient associations, investigators and hospital formulary committees;
- Are responsible for developing medical educational programs and disease awareness activities (alone or in partnership with scientific societies and/or patient associations);
- Are the contact point for investigator initiated research/studies (pre-clinical, clinical, non-interventional, etc);

- Are responsible, alone or in coordination with the medical information colleague, for answering to queries (from healthcare professionals or patients).

Medical Affairs activities are present throughout different moments of a medicine life cycle, such as pre-, peri- and post-launch and even post-LOE (lost of exclusivity):

- Prior to the commercialization of a new medicine, it is crucial to establish a KOL strategy to support the product launch. Medical Affairs colleagues must identify potential KOLs and foster interactions, providing available scientific information about the new medicine, including ongoing and upcoming studies. They should also perform disease awareness and discuss the appropriate treatment guidelines.
- At the time of launch, they must effectively communicate the adequate use of the new drug, according to the approved indications, and address the results from clinical studies, adverse events profile, dosing regimen and specific drug attributes.
- After the launch of a new drug, the Medical Affairs team can get in touch with key customers and retrieve feedback about the product, fine tune the communication of data about the new drug or addressing lacking information (developing phase IV studies, real world studies or investigator initiated research, that can be useful to differentiate the product from its competitors).
- When the end of the drug's life cycle is close, they are also responsible for putting in place a KOL disengagement strategy, whether transitioning the KOL to another business unit or progressively reducing the number of interactions with him/her, until a new drug is advancing on the pipeline and enters a phase II/III clinical development.

Considering the growing importance of Medical Affairs teams, as both internal and external customers increasingly recognize they are the most knowledgeable individuals to talk about a medicine within a pharmaceutical company, and they are an independent, reliable and trustworthy source of information, capable of developing long-term, peer-to-peer relationships with healthcare professionals, the value of such team for a pharmaceutical company cannot be dismissed. It will continue to positively impact the business.

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